

March 19, 2003:1065-9

In contrast to these clearly semiquantitative results, we found a direct, logarithmic, and quantitative relationship between E/A ratio and PA pressure measured as continuous variables in patients with CTEPH. We also documented a similar direct relationship between E/A and cardiac output in the same group. The results of our study expand upon previous studies that have reported on abnormal LV diastolic function in patients with chronic pulmonary hypertension. However, it is still difficult to hypothesize that abnormal LV diastolic filling contributes significantly to dyspnea in these patients. In fact, pulmonary capillary wedge pressure increased slightly from 9.8 ± 5 to 11.5 ± 4.5 mm Hg ($p = 0.04$) after PTE. This suggests that dyspnea in patients with severe pulmonary hypertension is unlikely to be related to an elevated LV filling pressure.

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doi:10.1016/S0735-1097(02)03016-4

REFERENCES

1. Mahmud E, Raisinghani A, Hassankhani A, et al. Correlation of left ventricular filling characteristics with right ventricular overload and pulmonary artery pressure in chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol* 2002;40:318-24.
2. Moustapha A, Kaushik V, Diaz S, Kang S-H, Barasch E. Echocardiographic evaluation of left-ventricular diastolic function in patients with chronic pulmonary hypertension. *Cardiology* 2001;95:96-100.
3. Dittrich HC, Chow LC, Nicod PH. Early improvement in left ventricular diastolic function after relief of chronic right ventricular pressure overload. *Circulation* 1989;80:823-30.
4. Dittrich HC, Nicod PH, Chow LC, Chappuis FC, Moser KM, Peterson KL. Early changes of right heart geometry after pulmonary thromboendarterectomy. *J Am Coll Cardiol* 1988;11:937-43.

Detrimental Effects of Late Artery Opening

In reference to the recent study by Yousef et al. (1) in the *Journal*, we agree that percutaneous coronary interventions (PCI) for an occluded artery late after an acute myocardial infarction are not risk-free procedures, and even an immediate angiographic success may be harmful in the long term. The investigators attribute detrimental effects of late reperfusion—significantly greater one-year left ventricular (LV) end-systolic and end-diastolic volumes—to periprocedural microembolization of collateral vessels. However, as reported in the study limitations, the researchers did not routinely measure cardiac markers after PCI; therefore, no proof for such a causative mechanism exists.

An alternative explanation for this finding is that the adverse effect on remodelling of the invasive strategy is not related to the PCI procedure itself but to the extremely high rate of late events occurring in these patients in relation to a suboptimal treatment. Here the 50% rate of adverse event at one year is far higher than the 32% rate reported after stent implantation in occluded arteries, even using the now outdated Palmaz-Schatz stents and warfarin therapy (2). The use of NIR stents (3) and the suboptimal (two weeks) duration of clopidogrel therapy might be advocated as a

cause of higher-than-expected restenosis and reocclusion rates in the study by Yousef et al. (1).

Moreover, LV volumes are certainly a better surrogate end point than exercise tolerance, but improvements in exercise duration and peak rate-pressure products in the intervention group are unexpectedly discordant from echocardiographic findings. Changes in mitral regurgitation severity may contribute to limitation of exercise capacity (4). The assessment of mitral regurgitation in this setting could be extremely helpful in clarifying whether detrimental effects on remodelling are uniformly found in the entire cohort of patients who underwent PCI or only in the subgroup of patients who experienced adverse events.

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REFERENCES

1. Yousef ZR, Redwood SR, Bucknall CA, et al. Late intervention after anterior myocardial infarction: effects on left ventricular size, function, quality of life and exercise tolerance. Results of The Open Artery Trial (TOAT study). *J Am Coll Cardiol* 2002;40:869-76.
2. Rubartelli P, Niccoli L, Verna E, for the GISSOC investigators. Stent implantation versus balloon angioplasty in chronic coronary occlusions: results from the GISSOC trial. *J Am Coll Cardiol* 1998;32:90-6.
3. Hoffmann R, Mintz GS, Haager PK, et al. Relation of stent design and stent surface material to subsequent in-stent intimal hyperplasia in coronary arteries determined by intravascular ultrasound. *Am J Cardiol* 2002;89:1360-4.
4. Lapu-Bula R, Robert A, Van Craeynest D, et al. Contribution of exercise-induced mitral regurgitation to exercise stroke volume and exercise capacity in patients with left ventricular systolic dysfunction. *Circulation* 2002;106:1342-8.

REPLY

Zimarino et al. have based their conclusions on a comparison of events between the TOAT (1) and GISSOC (2) studies. This comparison is not justified as neither study was powered to examine clinical end points. Furthermore, the inclusion criteria of the trials differed. For example, only 50% of the stented patients within GISSOC had a prior myocardial infarction, whereas in TOAT this was 100%. Moreover, to increase the prevalence of adverse remodelling, the eligibility criteria of TOAT ensured that the stented vessel subtended a large volume of infarcted myocardium with a presumed high microvascular resistance and thus more disordered flow. In addition, 28% of events within TOAT comprised heart failure and stroke, end points that are unlikely to be related to reocclusion. Omitting these end points results in a one-year event rate of 24% in those randomized to intervention,

compared to a nine-month event rate of 32% in the corresponding patients within GISSOC.

Undoubtedly, as stent designs improve, late complications will become less frequent; thus, use of drug-eluting stents (3) in TOAT and GISSOC could have resulted in fewer restenoses and reocclusions. The use of post-stent clopidogrel and other thienopyridines for only two weeks is validated and supported by Mishkel et al. (4) and Berger et al. (5).

Unfortunately, Doppler color flow mapping was not a protocol requirement in our study; therefore, quantitative assessment of resting mitral regurgitation is incomplete. Nevertheless, because all patients had single-vessel disease with left anterior descending artery occlusion, the posterior papillary muscle is likely to have been spared, making annular dilation the most probable mechanism of mitral incompetence. We agree that the increased exercise endurance observed in open-artery patients (despite increased left ventricular volumes) is paradoxical, and likely to be mediated through a placebo effect.

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REFERENCES

1. Yousef ZR, Redwood SR, Bucknall CA, et al. Late intervention after anterior myocardial infarction: effects on left ventricular size, function, quality of life and exercise tolerance. Results of The Open Artery Trial (TOAT study). *J Am Coll Cardiol* 2002;40:869-76.
2. Rubartelli P, Niccoli L, Verna E, for the GISSOC investigators. Stent implantation versus balloon angioplasty in chronic coronary occlusions: results from the GISSOC trial. *J Am Coll Cardiol* 1998;32:90-6.
3. Morice MC, Serruys PW, Sousa JE, et al. A randomised comparison of a sirolimus-eluting stent with standard stent for coronary revascularisation. *N Engl J Med* 2002;346:1773-80.
4. Mishkel GJ, Aguirre FV, Ligon RW, Rocha-Singh KJ, Lucore CL. Clopidogrel as adjunctive antiplatelet therapy during coronary stenting. *J Am Coll Cardiol* 1999;34:1884-90.
5. Berger PB, Mahaffey KW, Meier SJ, et al. Safety and efficacy of only 2 weeks of ticlopidine therapy in patients at increased risk of coronary stent thrombosis: results from the Antiplatelet Therapy alone versus Lovenox plus Antiplatelet therapy in patients at increased risk of Stent Thrombosis (ATLAST) trial. *Am Heart J* 2002;143:841-6.

Specificity of Noninvasive Pacemaker Stress Echocardiography in Diagnosis of Coronary Artery Disease

We read with great interest the recently published study by Picano et al. (1) in the October 2, 2002, issue of *JACC*. The investigators concluded that noninvasive pacemaker stress echocardiography is a diagnostically efficient method for patients with a permanent

pacemaker and suspected or known coronary artery disease (CAD).

Nevertheless, some concerns arise based on our experience and from careful review of the published reports.

First, the main problem in detecting CAD in patients with permanent ventricular pacing is the low specificity of noninvasive techniques related to abnormalities of microvascular flow arising from chronic functional and/or structural abnormalities induced by abnormal ventricular excitation (2). We do not believe that the study by Picano et al. (1) could solve this problem; the studied group consisted of patients with a high prevalence of risk factors for CAD (>50%) and/or previous myocardial infarction (37%): it was, therefore, an excellent way to assess the sensitivity of the method, but not the specificity. In addition, 15 of 45 patients were in AAI pacing mode, and even for the remaining patients we do not know if there was partial or full ventricular excitation from the pacemaker electrode during daily life or during the stress protocol. We also do not know whether the studied group represents a total population of patients with a pacemaker, as the manner of the patients' recruitment is unclear.

Second, the allegation that perfusion defects are more common than wall motion abnormalities during stress in patients with alterations of coronary flow reserve and normal epicardial coronary arteries conflicts with the findings of a study by Tse et al. (3), who observed wall motion abnormalities by radionuclide ventriculography to occur in the same proportion of patients with permanent ventricular stimulation and no significant CAD as did perfusion defects detected by dipyridamole thallium myocardial scintigraphy. Thus, the advantage of the stress echocardiogram remains in question.

Third, given the deterioration of myocardial perfusion over time that is observed in some studies (3,4), it is crucial to know the mean duration of pacing, especially in patients without wall motion abnormalities. Such data were not provided in the study by Picano et al. (1).

In conclusion, although no one has doubt about the diagnostic accuracy of the noninvasive pacemaker stress echocardiogram in patients with AAI pacing mode, or, more generally, about the sensitivity of the same method in detecting CAD, the specificity of the method remains in doubt. Based on data currently available, a specificity of 50% is the best we can expect from noninvasive techniques (2-5), at least in patients with permanent ventricular stimulation.

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doi:10.1016/S0735-1097(02)02978-9

REFERENCES

1. Picano E, Alaimo A, Chubuchny V, et al. Noninvasive pacemaker stress echocardiography for diagnosis of coronary artery disease. *J Am Coll Cardiol* 2002;40:1305-10.